

### **REMARKS**

New claims 105-119 have been added. Support for new claims 105-119 can be found throughout the specification, for example, on page 10, lines 16-22; page 11, lines 22-25; page 12, lines 24-27; page 13, lines 11-16; page 14, lines 14-15; page 14, lines 23-24; and page 16, lines 3-6.

Claims 28-47 and 105-119 are now pending for examination.

#### **Rejections under 35 U.S.C. §103(a) with respect to Hill in view of Charych**

Claims 28-33, 36, 41, and 43-47 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Hill, *et al.*, U.S. Patent No. 5,496,452 ("Hill") in view of Charych, *et al.*, U.S. Patent Application Publication No. 2002/0055125 ("Charych"). The Office Action alleges that Hill teaches immobilizing enzymes on biosensors to measure toxins, and that BSA can be used as a linker. The Office Action also alleges that Charych teaches a proteomic microarray assay having a density of spots from 1 to 5,000 spots per cm<sup>2</sup>. The Office Action concludes by stating "Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided the method [of] Hill, et al., with the device and coupling target specific antibody as taught by Charych et al. since an efficient throughput analysis is of great demand in studying protein complex field. (See Section 0007)."

To begin with, Applicants do not concede that Charych is properly prior art to the Applicant's claimed inventions. Applicants reserve the right to establish an invention date for the claimed invention that is on or before the effective 35 U.S.C. §102(e) date of the subject matter of Charych relied on in the Office Action.

The Office Action does not point to a suggestion or motivation to combine Hill and Charych in the manner suggested in the Office Action, that can withstand scrutiny for the reasons indicated below. The Office Action points to paragraph 0007 in Charych, which states, "Thus, there is an overwhelming need to develop effective microarray technology that is useful in a protein context," and describes the difficulties in detecting proteins. However, a statement that merely states that there exists an overwhelming need to develop technology does not provide any

guidance to one of ordinary skill in the art, in viewing Charych, as to how or why to modify Hill in view of Charych along the lines suggested in the Office Action. Hill describes immobilizing enzymes on biosensors, but does not disclose or suggest microarrays. The Office Action has not pointed to a disclosure or suggestion in Charych to modify the biosensor device of Hill to include the microarray of Charych. Additionally, as pointed out below, one of ordinary skill in the art, at the time Applicants' invention was made, would not have been motivated to modify the biosensor device of Hill in the manner suggested in the Office Action. Thus, the Office Action has not provided a *prima facie* case of obviousness with Hill in view of Charych. Furthermore, one of ordinary skill in the art, at the time Applicants' invention was made, would have recognized that the use of a microarray as described in Charych in the context of a biosensor as described in Hill would have added no additional benefit or functionality to Hill, and instead would have rendered the Hill biosensor unsuitable or more poorly suited for performing its intended purpose.

Specifically, Hill describes a biosensor for the detection and determination of the concentration of toxins by the use of an enzyme inhibition assay. In this biosensor, an enzyme (e.g., horseradish peroxidase) is oxidized by hydrogen peroxide and reduced by an electron transfer agent (e.g., ferrocene). The enzyme oxidation-reduction reaction is detected using a single electrode to which the enzyme has been immobilized. Toxins that the biosensor is sensitive to affect the electron transfer agent in this reaction, thus allowing the electrode to detect the presence of the toxin. (See, e.g., the abstract.) Charych, on the other hand, discloses a substrate having a large number of protein-binding spots on a substrate. The proposed modification of Hill in view of Charych would, therefore, result in a substrate, functioning as an electrode, in which a plurality of enzymes have been immobilized thereon in protein-binding spots. Analytes binding to enzymes located on the substrate would be detected by a change in the voltage of the electrode. However, such a biosensor would be incapable of distinguishing between the binding of different analytes to the various protein-binding spots, as the disclosed electrode can only determine a net electrical voltage, and cannot spatially resolve the location of individual spots on the substrate. Thus, as the microarrayed spots of such a device would be

completely nonfunctional for their intended purpose (i.e. for enabling the ability to differentially detect, spatially resolve, and identify a plurality of analytes), it is believed that there would have been, at the time Applicants' invention was made, no motivation to make the combination of Charych and Hill.

Moreover, Hill describes the binding of enzymes to BSA attached to the electrode, i.e., it is desired that the enzymes are bound to BSA. Charych, on the other hand, refers to BSA as a blocking agent, i.e., Charych describes the binding of BSA only to the continuous, uncoated regions of the substrate that remain after spotting with other materials (see e.g., paragraph 0098). Thus, Charych providing the BSA only in regions of the substrate where the binding of protein is *not* desired (i.e., to *prevent* protein binding thereto), essentially opposite the purpose for which BSA is employed in Hill. Thus, by teaching two diametrically opposed functionalities and purposes for the BSA employed the two references teach away from the proposed combination. Therefore, as the combination of Charych and Hill would be less useful than Hill or Charych maintained separately and the references themselves effectively teach away from the proposed combination, it is believed that one of ordinary skill in the art would have had no motivation to make the combination.

For at least the above-described reasons, it is believed that the combination of Hill and Charych is improper, and thus, Applicants respectfully request that the rejection of claims 28-33, 36, 41 and 43-47 be withdrawn for at least these reasons.

Rejections under 35 U.S.C. §103(a) with respect to Hill in view of Charych and Kato

Claims 34, 35, and 37-40 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Hill in view of Charych, and further in view of Kato, *et al.*, U.S. Patent No. 4,507,234 ("Kato"). The Office Action alleges that while Hill and Charych together render obvious independent claim 28 from which dependent claims 34, 35, and 37-40 each depend, the references "do not explicitly teach using covalent binding to couple with BSA and the protein," as recited in claims 34, 35, and 37-40, which limitations are taught in Kato. Accordingly, the basis for this rejection is that Hill and Charych render obvious an array meeting all of the

limitations of claims 34, 35, and 37-40, except for the specific limitations added in those claims. The Office Action asserts that it would have been obvious to combine Hill, Charych, and Kato.

For at least the reasons discussed above with respect to the above rejection under 35 U.S.C. §103(a), the premise of the rejection (that Hill and Charych render obvious all of the limitations of independent claim 28) is incorrect. As discussed above, Hill and Charych do not render obvious the invention recited in claim 28, from which claims 34, 35, and 37-40 ultimately depend. Accordingly, while Applicants do not concede that there would have been any motivation to combine Hill, Charych, and Kato as suggested in the Office Action, or that the proposed combination would include all of the limitations of the rejected claims, the present basis of the rejection cannot stand. Thus, Applicants respectfully request withdrawal of the rejection of claims 34, 35, and 37-40, for at least these reasons.

Rejections under 35 U.S.C. §103(a) with respect to Hill in view of Charych and Patron

Claim 42, which indirectly depends from independent claim 28, has been rejected under 35 U.S.C. §103(a) as being unpatentable over Hill in view of Charych and Patron, *et al.*, U.S. Patent Application Publication No. 2001/0041349 ("Patron"). The Office Action alleges that while Hill and Charych render obvious independent claim 28 from which dependent claim 42 depends, the references "fails to specifically teach using poly-histidine-metal interaction as the protein/BSA binding method," as recited in claim 42, which limitation is taught in Patron. Accordingly, the basis for this rejection is that Hill and Charych render obvious an array meeting all of the limitations of claim 42, except for the limitation added in claim 42 directed to a poly-histidine-metal cation interaction. The Office Action asserts that Patron discloses such an interaction, and that it would have been obvious to combine Hill, Charych, and Patron.

To begin with, Applicants do not concede that Patron is properly prior art to the Applicants' claimed inventions. Applicants reserve the right to establish an invention date for the claimed inventions that is on or before the effective 35 U.S.C. §102(e) date of the subject matter of Patron relied on in the Office Action.

For at least the reasons discussed above with respect to the above rejection under 35 U.S.C. §103(a), the premise of the rejection (that Hill and Charych render obvious all of the limitations of claim 42, other than a poly-histidine-metal cation interaction) is incorrect. As discussed above, Hill and Charych do not render obvious the invention recited in claim 28 and 33, from which dependent claim 42 depends. Accordingly, while Applicants do not concede that there would have been any motivation to combine Hill, Charych, and Patron in the manner suggested in the Office Action, or that the proposed combination would include all of the limitations of the rejected claims, the present basis of the rejection cannot stand. Thus, Applicants respectfully request the withdrawal of the rejection of claim 42 for at least these reasons.

#### New Claims

New claims 105-119 have been added. Claim 105 is in independent form and is directed to an article comprising a polymer that is immobilized on a solid support and that is configured to become specifically attached to a chemically unmodified protein. Nowhere is it observed that the prior art of record discloses, suggests, or motivates an article comprising a polymer that is immobilized on a solid support and that is configured to become specifically attached to a chemically unmodified protein. Accordingly, newly added independent claim 105 is believed to patentably distinguish the references of record.

New claims 106-119 depend from and include all of the limitations of independent claim 105, and are believed to patentably distinguish the references of record for at least the same reasons as claim 105.

**CONCLUSION**

In view of the foregoing remarks, Applicants believe that this application is in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicants' attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

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